

### REMARKS

This document is filed in reply to the Office Action dated September 8, 2004 ("Office Action"). Claims 1-36 are pending. Claims 10-22 have been withdrawn from further consideration for being drawn to a non-elected invention. Claims 1-9 and 23-36 are now under examination. Reconsideration of this application is requested in view of the following remarks:

#### Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-9 and 23-36 for containing new matter. According to her, "the newly added limitation 'unlabelled' discrimination primer [to independent claims 1 and 23] has no support in the specification." See the Office Action, the paragraph bridging pages 5 and 6.

In the last response filed on June 3, 2004, Applicants already pointed to the supporting passage in the specification. See that response, page 8, lines 4-5 and footnote 1 therein. In this connection, Applicants would like to remind the Examiner that she previously raised an almost identical rejection in the advisory action dated September 3, 2003. Applicants subsequently filed a Request for Continued Examination and identified the passage that supports an unlabelled discrimination primer. In the following office action dated December 3, 2003, the Examiner did not maintain the rejection. In other words, she in effect withdrew this rejection. For the reasons set forth above, Applicants submit that the limitation at issue is supported by the specification.

#### Rejection under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of all claims being examined for obviousness on two grounds. Applicants respectfully traverse:

#### I

Claims 1-4, 6-8, 23-26, 30, and 32-36 remain rejected as being obvious over U.S. Patent No. 6,156,503 to Drazen et al. ("Drazen") in view of Ugozzoli et al. (GATA, 1992, Vol. 9(4), pp. 107-112; "Ugozzoli"). See the Office Action, page 3, lines 16-18. Applicants disagree and discuss independent claims 1 and 23 first.

Claim 1 covers a discrimination primer for PCR amplification that includes, among others, a mismatch at the penultimate position from its 3' end and a first binding member, which binds to a second binding member. Ugozzoli teaches a primer for primer extension having a 5' X portion that is complementary to an immobilized, pre-selected nucleic acid sequence. According to the Examiner, the 5' X portion and the pre-selected nucleic acid sequence are equivalent to the first and second binding members, respectively. The Examiner contended that, in view of Drazen's teaching of an amplification primer that has a penultimate mismatch, a combination of the two references would suggest the claimed discrimination primer.

In the last response, Applicants pointed out that Ugozzoli's teaching, limited to primer extension, is not necessarily applicable to PCR amplification, since a functional extension primer may not work as a PCR amplification primer to generate specific amplification products. Thus, one skilled in the art would not have combined the teachings from Ugozzoli and Drazen in the manner proposed by the Examiner.

The Examiner refused to accept this view on the ground that "[claim 1 is] drawn to the product, which is [a] ... discrimination primer." In other words, she believed that claim 1 covered both PCR amplification primers and extension primers. Applicants would like to point out that claim 1 is specifically limited to a discrimination primer for PCR amplification only, and does not cover that for primer extension. As admitted by the Examiner, "[t]he motivation [for combining Ugozzoli and Drazen] is that by using the [Ugozzoli 5' X portion], it allows the primer-extension product to be immobilized ..." (emphasis added). That is, one skilled in the art would have been motivated to apply Ugozzoli's teaching only to a extension primer but not to a PCR amplification primer as covered by claim 1.

In the last response, Applicants also presented a Declaration by Dr. Shin-Hwan Wang showing that a primer having the above-mentioned Ugozzoli 5' X portion did not work as a PCR amplification primer to generate specific amplification products, while a primer disclosed in the instant application (SEQ ID NO: 2) worked. The Examiner countered that the declaration "is insufficient ... because [SEQ ID NO: 2] is not cited in claim 1." See the Office Action, page 4, lines 10-15.

Applicants disagree. The Examiner appeared to incorrectly believe that the declaration was submitted to present an unexpected result from using SEQ ID NO: 2, and concluded that the unexpected result was not commensurate in scope with claim 1. As a matter of fact, the declaration was submitted to show the effect of the Ugozzoli 5' X portion on a PCR primer. See the last response, page 10, paragraph 3. As the declaration clearly shows a primer having the Ugozzoli 5' X portion did not work as a PCR amplification primer, it sufficiently supports the proposition that one skilled in the art would not have been motivated to apply Ugozzoli's teaching to a PCR amplification primer covered by claim 1. In other words, the declaration only serves to show that the Examiner's reliance on Ugozzoli is misplaced, and as a result, she has failed to establish a prima facie obviousness.

In view of above remarks, Applicants submit that claim 1 is not rendered obvious by Drazen and Ugozzoli. Claim 23 covers a kit that contains the discrimination primer of claim 1. For the same reasons set forth above, it is also non-obvious over these two references. So are claims 2-4, 6-8, 24-26, 30, and 32-36, all of which depend from claims 1 and 23.

## II

The Examiner maintained the rejection of claims 5, 9, 27-29, and 31, which depend from claim 1 or 23, as being obvious over Drazen in view of Ugozzoli and U.S. Patent No. 6,383,742 to Drmanac et al. ("Drmanac"). See the Office Action, page 4, lines 15-16.

In the last response, Applicants pointed out: (i) the three cited references would suggest a **labeled** primer and (ii) the discrimination primer recited in claim 1 and the first primer recited in claim 23 are **unlabeled**. Thus, the three references teach away from claims 1 and 23, as well as claims 5, 9, 27-29, and 31 depending from them. In the Office Action, the Examiner alleged that "there is a second primer cited in claim 28, which is labeled at the 5' end. ... Thus the combination of the reference renders claims [5, 9, 27-29, and 31] obvious and the rejection is maintained."

Claim 28, dependent from claim 23, covers a kit that contains an **unlabeled first primer** and a **labeled second primer**. It appears to be the Examiner's position that the combination of

the three cited references would have suggested the labeled second primer, thereby rendering kit claims 27-29 and 31 obvious. Applicants would like to point out that, even if the combination would have suggested the labeled second primer, it would not have suggested the unlabeled first primer, let alone a kit containing it. As claims 27-29 and 31, all dependent from claim 23, are each drawn to a kit containing the unlabeled first primer, they are not rendered obvious by the combination of the three references. Claims 5 and 9, dependent from claim 1, each cover an unlabeled discrimination primer, which corresponds to the unlabeled first primer recited in claim 23. For the same reasons set forth immediately above, these two claims are also not rendered obvious by the combination of the three cited references.

#### CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that meets the written description requirement and is non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing the attorney docket 12674-003001.

Respectfully submitted,

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